UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/917,278	07/30/2001	Reginald M. Gorczynski	9579-39	9183

7590 08/08/2003

MICHELINE GRAVELLE
Bereskin & Parr
Box 401
40 King Street West
Toronto, ON M5H 3Y2
CANADA

EXAMINER	
ROARK, JESSICA H	
ART UNIT	PAPER NUMBER
1644	17

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/917,278	Applicant(s) GORCZYNSKI ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 5/21/03 (Paper No. 16), is acknowledged.
Claims 1-9 have been cancelled.
Claims 10-13 have been added and are under consideration in the instant application.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

Applicant's arguments with respect to claims 10-13 have been considered, but are moot in view of the new grounds of rejection.

3. It is noted that New Grounds of Rejection not necessitated by Applicant's amendment are set forth herein following further consideration of the disclosure.

Accordingly, this Office Action is non-Final.

4. Claims 10-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The specification provides a working example on pages 83-85 and Figure 24A showing that in mice pre-immunized with a CD86 transfected form of leukemic cells prior to challenge with the wildtype leukemia, administration of an anti-CD200 (anti-OX-2) antibody at the time of wildtype tumor challenge improved survival. However, Figure 24A also shows that the effect was only seen in pre-immunized mice: administration of the antibody in mice without pre-immunization did not improve survival. In addition, the specification notes that no improvement of survival was seen when mice were pre-immunized with CD80 transfected cells, then challenged and given anti-OX-2 antibody.

The specification also provides a working example on pages 91-92 and Figure 30 showing that anti-OX-2 antibody could inhibit the enhancement of lung nodule formation that accompanied the administration of allogeneic leukocytes following I.V. administration of cultured sarcoma cells. However, Figure 30A also shows that administration of anti-OX-2 was not by itself sufficient to reduce the number of lung nodules compared to PBS alone, and Figure 30B shows that the percentage of mice showing no lung nodules after tumor cell administration was actually decreased compared to administration of PBS.

Thus although the specification does provide two examples in which tumor growth was inhibited by an antibody to the Ox-2 (CD200) molecule, the results appear to be limited to a highly specialized set of circumstances. In neither the pre-immunization model nor the lung nodule formation model did simple administration of the anti-OX-2 antibody appear to have a beneficial effect.

Given these limited results, without more direct support the skilled artisan would not consider it predictable that the data provided in the instant disclosure could be generalized. In addition, the scope of instant claims 10, 11 and 13 encompasses methods of treating *any* cancer, and although claim 12 recites particular cancers, these are recognized in the art to be highly diverse.

The state of the art recognized that treatment of cancer, particularly diverse types of cancers by the same approach, was highly unpredictable. For example, the art recognized that treatment of cancers of the blood versus treatment of solid tumors was subject to very different requirements regarding delivery of therapeutics. While cancers of the blood are exposed to intravenously administered agents such as antibodies, solid tumors present a far more formidable challenge to delivery of therapeutics. Jain (Nature Medicine 1998; 4(6):655-657) reviews that delivery of therapeutics to solid tumors is inhibited by the disorganized tumor vasculature, the heterogeneity in vascular permeability in a solid tumor, and the relatively high pressure found within a solid tumor that forces interstitial fluid and therapeutics therein out of the tumor (see "Progress in Understanding the Barriers", page 655).

In addition, even when data has been provided suggesting that antibody therapy of a particular tumor type was effective in animal models of particular types of cancers, the state of the art recognized that it was unpredictable if success in one or a limited number of models could be generalized for other types of cancer. For example, despite encouraging results in certain animal models of cancer using antibodies to the molecule 4-1BB, Kim et al. (Cancer Res. 2001; 61:2031-2037) review that the immunogenicity of the tumor and its anatomical location are both important in determining whether that particular tumor will be responsive to antibody administration (see e.g., the Discussion on pages 2035-2036). Similarly, Kjaergaard et al. (Cancer Res. 2000; 60:5514-5521) found that the efficacy of an antibody to the OX-40 receptor also was effected by the intrinsic immunogenicity of the tumor, its anatomical location, and the tumor burden (e.g., as summarized in the Abstract).

Further, it was well known in the art at the time the invention was made that eliciting protective immunity in animals *prior to tumor challenge* is not reasonably predictive that a therapy will also be therapeutic, i.e., capable of reducing *an established tumor burden*. For example, Boon (Adv. Cancer Res. 1992; 58:177-210) states: when one considers moving from active immunization in animals to similar procedures in cancer patients, there is an important point that must not be overlooked. For experimental antitumoral immunization in animals, one usually immunizes a normal animal and the effect is evaluated by the resistance to a tumor cell. For human patients, we will have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have occurred and it may prevent immunization (page 206, 2nd paragraph).

Thus in view of the unpredictability associated with the field of monoclonal antibody therapy of cancer and the ambiguous data of the instant disclosure, there does not appear to be enabling support for "a method of treating a cancer" or for a method of reducing tumor cell growth. The data used to support enablement of a method of treating cancer or inhibiting growth of a tumor should provide sufficiently consistent results using models sufficiently robust and diverse such that the skilled artisan would consider experimental results reasonably predictive of treating cancer in humans, and would consider the data to be commensurate in scope with the diversity of cancer types encompassed by the claims. Thus without further guidance, it would require further extensive and undue experimentation of the skilled artisan to practice the instant methods, particularly with respect to the diverse cancers recited in claim 12.

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
August 7, 2003

PHILLIP GAMBEL
PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
8/7/03